REVIEW ARTICLE

Philanthropies as partners for drug development in public–private partnerships

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Abstract: Disease-focused philanthropic organizations play an increasing role in the strategy and conduct of biomedical research, with many focusing on drug development for specific diseases and patient populations. More and more they not only provide resources and expertise, but also take active part managing the strategy and objectives of targeted research programs, using approaches such as venture philanthropy. Many also lead and participate in public–private partnerships. One example is the partnership between the Polycystic Kidney Disease (PKD) Foundation and the Critical Path Institute (C-Path) which brings together several pharmaceutical companies and academic institutions to develop new broadly-used biomarkers. Another case is the partnership between JDRF (formerly known as the Juvenile Diabetes Research Foundation) and the Innovative Medicines Initiative (IMI), involving financial support of the IMIDIA project (Innovative Medicines Initiative for Diabetes) which is focused on improving beta-cell function and identifying biomarkers for diabetes treatment monitoring. These examples show that in addition to providing financial support and expertise, philanthropic foundations are also in a unique position to coordinate the patient and research communities to enable and accelerate specific medicines development projects.

Keywords: philanthropic foundation, venture philanthropy, polycystic kidney disease, type 1 diabetes

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Received: May 13, 2015; **Accepted:** May 30, 2015; **Published Online:** June 12, 2015

Citation: Lim M D, Brumfield M A and Goldman M, 2015, Philanthropies as partners for drug development in public–private partnerships. *Journal of Medicines Development Sciences*, vol.1(1): 10–13. http://dx.doi.org/10.18063/JMDS.2015.01.002.

1. Introduction

Translational biomedical research has always depended on collaborations based on resources and expertise brought by each partner to advance an initial finding to clinical application. Traditionally, many of these partnerships focused on advancing a single product or were extracurricular activities that evaluated early-stage concepts. While these efforts continue to dominate the biomedical landscape, the past decade has also witnessed the emergence of over 400 research consortia. This model of partnership temporarily combines the resources and expertise of multiple stakeholders to develop a shared tool or asset, with an aim to advance the efforts of its partners and those of the broader scientific community[1].

Research consortia aim to reduce the risk of innovating methods for discovering and manufacturing medical products, as well as standardize processes in a highly regulated industry[2]. At first glance, the mission statements of government agencies, academic research institutions, and private-sector drug development would seem to have more differences than similarities. However, the multitude of drug development partnerships indicates the diversity of synergies leveraged to address each stakeholder's unique vulnerabi-

lities. For example, with 64% of global spending into drug development coming from only 20 companies[3], the entire biopharmaceutical sector is sensitive to changes in regulatory policy and market forces that affect a single company, in addition to the overall scientific and clinical challenges for developing drugs. At the same time, regulatory agencies often do not have the resources to stay ahead of drug development science, finding themselves ill-prepared to evaluate the safety and efficacy of product candidates based on next-generation technologies. In addition to regulating medical products, other government biomedical agencies play multiple roles to advance society through the preservation of public health, advancement of economic competitiveness, and sustaining innovation. As shown by the recent Ebola outbreak and continuing challenges such as Alzheimer's disease, government agencies lack the capability to single-handedly advance drug and vaccine development against complex diseases and are increasingly focusing their resources to catalyze public–private partnerships that expand the impact of their limited taxpayer dollars, rather than finding ways to integrate independent and individually-funded research efforts[4–6].

2. The Role of Philanthropic Foundations

Another biomedical research stakeholder with increasing influence is the disease-focused philanthropic foundation. With over 200,000 philanthropies operating in Europe and the US, the majority of these not-for-profit organizations derive their finances from donated personal assets or fundraising. Most are driven by altruism and a sense of social responsibility across a wide field of interests—two-thirds have a health-related focus[7]—and distribute their funds as charitable gifts. A subset of philanthropies focus on advancing drug development for specific diseases and patient populations[8], many of which leverage their resources and expertise through an investment approach known as venture philanthropy[9]. Instead of providing a grant or gift to a researcher, this model of impact investing gives a philanthropy the ability to proactively manage the strategy and scientific objectives of a research program in collaboration with their partner. These investments often include conditions for financial recovery to ensure sustainability and support of further research in their disease or condition of interest[10].

In addition to directly supporting a single research organization, many disease-focused venture philanthropies further diversify their portfolio by leveraging public–private partnerships to broadly advance drug development. Non-profit foundations are considered as neutral parties that focus only on improving the lives of a specific patient population, regardless of a specific company or product, and can serve as safe-harbor conveners between multiple drug development companies and government regulators. The scope of consortia that involve participation of philanthropies cover the whole research and development process (Table 1), all with the assumption that new and broadly-usable tools would catalyze entry of multiple companies into a specific and oftentimes neglected disease area. For example, diagnostic/prognostic biomarkers that can be used to stage a disease or track its progression are often not available or are poorly-validated, an absence of evidence that creates a scientific hurdle and unclear regulatory pathway. Consortia which convene regulatory scientists with companies that use similar approaches for developing drugs act as a forum for open collaboration, often to develop standardized and non-product-specific tools that aid regulatory evaluation. By combining the collective knowledge of their internal staff and funded investigators with the resources and expertise of the broader research community, foundations also have a unique position to lead clinical biomarker studies that address drug development needs, designed in a manner sensitive to the lifestyle challenges of their patient populations. Foundations can also coordinate patient populations who already support their mission to power and execute longitudinal natural history studies, often in concert with industry supporters who lack the resources and expertise to conduct these essential studies on their own. As public–private partnerships, the data generated by these consortia are often made available to the wider scientific community. The outcome of these opportunities is not to improve the chance of success for a single company, but to bring benefit to a whole patient population.

3. Polycystic Kidney Disease Foundation and C-Path

In many instances, foundations are responsible for setting the scientific agenda and convening stakeholders to further develop and initiate a research consortium. For example, one strategy for the US-based Polycystic Kidney Disease (PKD) Foundation is to develop shared tools such as surrogate endpoint measures to incentivize industry investment into novel treatment options for autosomal dominant polycystic kidney disease (ADPKD)[11]. This genetic disease is suffered by millions across the globe with more than

Table 1. Examples of drug development consortia with philanthropic stakeholders

Consortium	Philanthropy	Management Organization	Purpose
Critical Path to TB Drug Regimens	Bill and Melinda Gates Foundation, TB Alliance	Critical Path Institute	Develop data standards, qualify biomarkers for regulatory application, develop natural history models
Multiple Sclerosis Outcome Assessments Consortium	National Multiple Sclerosis Society	Critical Path Institute	Qualification of clinician-reported outcome (ClinRO) assessments
Polycystic Kidney Disease Outcomes Consortium	Polycystic Kidney Disease Foundation	Critical Path Institute	Develop data standards and qualify imaging biomarkers for regulatory application
Accelerating Medicines Partnership: Rheumatoid Arthritis and Lupus	Arthritis Foundation, Lupus Foundation of America, Alliance for Lupus Research, Rheumatology Research Foundation	Foundation for the National Institutes of Health	Develop biomarkers for diagnosis and drug development
Alzheimer's Disease Neuroimaging Initiative	Alzheimer's Association, Alzheimer's Drug Discovery Foundation	Foundation for the National Institutes of Health	Develop biomarkers that diagnose patients with Alzheimer's disease and monitor disease progression
The Lung Cancer Master Protocol	Friends of Cancer Research		Develop and implement a clinical trial model that uses a multi-drug, targeted screening approach to match patients
European Autism Interventions	Autism Speaks	Innovative Medicines Initiative	Create validated cellular assays, animal models, new fMRI methods with dedicated analysis techniques, and new PET radioligands, as well as new genetic and proteomic biomarkers for patient-segmentation or individual response prediction
Biomarkers for Type 1 Diabetes and Retinal Diseases	JDRF, Leona M. and Harry B. Helmsley Charitable Trust	Innovative Medicines Initiative	Develop predictive biomarkers of disease progression
Pertussis Vaccination Research	Bill and Melinda Gates Foundation	Innovative Medicines Initiative	Develop biomarkers indicating protective immunity to pertussis
Parkinson's Progression Markers Initiative	Michael J. Fox Foundation for Parkinson's Research		Develop biomarkers for Parkinson's disease progression

50% developing kidney failure by the age of 50. With the exception of one recently approved treatment, no other treatment has been proven to prevent or delay the progression of ADPKD. The accepted regulatory endpoint is estimated glomerular filtration rate (eGFR), which stays largely stable for most of the patient's life even though the kidneys continue to grow inexorably; the PKD Foundation identified a need to develop a more rigorous biomarker given the weakness of this gold standard. The PKD Outcome Consortium, formed between the foundation with the non-profit Critical Path Institute (C-Path) and several pharmaceutical companies and academic institutions, focused on demonstrating total kidney volume as a new prognostic biomarker, for use as inclusion criterion in clinical trials to identify patients likely to show clinically-relevant decline in kidney function during the duration of a trial[12]. Through the consortium, data from patient registries and longitudinal studies were contributed, standardized, and pooled to develop a quantitative model in support of the intended use of this new biomarker. The final deliverable of the consortium, evidence that aims to support qualification of this biomarker, was submitted in March 2014 to both the Food and Drug Administration (US FDA) and the European Medicines Agency (EMA) for their consideration.

4. JDRF and IMI

Another example of how a disease-based foundation provides leadership, funding and influence to facilitate advancement in drug development is provided by JDRF (formerly known as the Juvenile Diabetes Research Foundation), the largest non-profit foundation and funder of type 1 diabetes (T1D) research. The foundation established a relationship with the Innovative Medicines Initiative (IMI), a joint undertaking between the European Union and the European Pharmaceutical Industry Association (EFPIA) that creates and manages drug development consortia. In 2012, JDRF began a partnership with the IMI program, IMIDIA (Innovative Medicines Initiative for Diabetes), investing around €1,000,000 to better understand pancreas beta-cell biology and the natural mechanisms that control beta cell mass and function. JDRF also contributed more than €350,000 to the IMI SUMMIT (Surrogate markers for Micro- and Macro-vascular hard endpoints for Innovative diabetes Tools) project to further explore genetic markers for diabetes complications. For both of these efforts, JDRF joined IMI

at an early stage and played an essential role in setting the agenda and the terms for the call for proposals. For example, the foundation jointly organized a workshop with IMI called the "Patient Diabetes Focus Meeting" to explore R&D gaps in the diabetes area from the perspective of patient needs and challenges. This 2014 meeting triggered in-depth discussions between JDRF and IMI, leading to the participation of JDRF as an Associate Partner to IMI and co-coordinator/co-founder of the IMI 2 topic "Translational Approaches to Disease Modifying Therapy of Type 1 Diabetes Mellitus". This seven-year project would create a comprehensive interdisciplinary network of clinical and basic scientists in cooperation with pharmaceutical companies and other non-profit organizations to advance the prediction, staging, prevention, and arrest-of-progression of type 1 diabetes. The concept aims to create novel tools such as biomarkers, disease models, and clinical trial paradigms, all of which are currently under review with a plan to start in September 2015. In addition, a Patient Advisory Committee will be an integral component embedded in the partnership to ensure that the desires and needs of patients and their families are addressed throughout the program. Furthermore, JDRF is in active discussions with IMI and EFPIA partners on ongoing and upcoming initiatives aimed at understanding cause and progression of T1D and delivering next generation therapeutics. These include areas of diabetic kidney disease, encapsulation of insulin-producing cells and modulation of gut microbiome, in full alignment with the foundation's core mission to deliver life-changing therapies for individuals with T1D.

5. Conclusion

Disease-focused philanthropic organizations are essential thought-leaders with a unique stake in drug development. Foundations are in a unique position to coordinate both the patient and research communities in focused efforts that generate research findings for the entire community, a value proposition that goes beyond their ability to provide additional funding. As non-profit organizations with missions to improve the lives of their patient populations, the majority is not beholden to a specific product and they can leverage their neutral convening ability to bring together competing companies and regulatory scientists to address broad challenges in their disease or condition of interest. However as with other stakeholders, their ability to provide financial resources and dedicate subject matter expertise to research is also limited, and many have found opportunities to expand their impact by leading and participating in public–private partnerships such as research consortia. Ensuring that the entire research community benefits from the collective expertise, coordination of resources, and distribution of results raises the tide for all boats, a central principle shared by both research consortia and disease-focused foundations.

Conflict of Interest

Martha Brumfield is the President and CEO of the Critical Path Institute; Michel Goldman is the former executive director of the Innovative Medicines Initiative.

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